REMARKS/ARUGMENTS

Upon entry of this reply, claims 1, 3, 5, 11, 15, 17 and 20 will be amended, and claims 21-26 will be added, whereby claims 1-6 will be pending. Claims 1, 11, 13 and 20 are independent claims.

By the amendments herein, the claims have been amended to even more clearly denote Applicants' invention.

For example, claim 1 has been amended to even more clearly recite a cell capable of inducing cellular immunity, said cell comprising an *in vitro* reaction product of a complex with an antigen-presenting cell, said complex formed from interaction of a hydrophobized polysaccharide and an antigen.

Moreover, claims 3 and 15 has been amended to clarify that the hydrophobized polysaccharide can be a polysaccharide modified with an alkyl group bound to an hydroxyl group of the polysaccharide or a sterol residue. This is in accordance with Applicants' originally filed disclosure, such as disclosed at page 7, beginning at line 16.

Still further, claim 11 has been amended to even more clearly be directed to a method for preparing a cell capable of inducing cellular immunity comprising reacting *in vitro* a complex with an antigen-presenting cell, said complex formed form interaction of a hydrophobized polysaccharide and an antigen.

Still further, claim 20 has been amended to even more clearly be directed to an *in vitro* cell capable of inducing cellular immunity, said *in vitro* cell comprising a complex comprising a combination of a hydrophobized polysaccharide, an antigen and an antigen-presenting cell.

Still further, claims 5 and 17 have been amended to even more clearly recite that the hydrophobized polysaccharide is a polysaccharide modified with a sterol residue, and the sterol residue is cholesterol residue.

Moreover, the newly added claims provide recitation in accordance with subject matter such as disclosed beginning at page 6, in the section labeled "(2) Hydrophobized polysaccharide".

Reconsideration and allowance of the application are respectfully requested.

Discussion of April 18, 2005 Interview

Applicants express appreciation for the courtesies extended by Examiner Ewoldt and Supervisory Patent Examiner Chan with Applicants' representative during an April 18, 2005 interview at the Patent and Trademark Office.

During the interview, the background of Applicants' invention and differences over the prior art were discussed. The examiners' attention was directed to the discussion of hydrophobized polysaccharide in the specification. In particular, it appeared that hydrophobized polysaccharide was being broadly construed in the Final Office Action as including any polysaccharide; however, arguments were presented that both the prior art and Applicants' specification provide a discussion of hydrophobized polysaccharide. The examiners appeared to be persuaded by these arguments that hydrophobic polysaccharide is different from a broad disclosure of a polysaccharide.

However, the examiners noted that Kohno discloses SBP-P which is a protein conjugated polysaccharide. The examiners contended that the pullulan would be hydrophobized by having a protein conjugated thereto, such as disclosed beginning at

the bottom of the left-hand column on page 213 of Kohno. Moreover, it was asserted that APC is added to this conjugate, such as on page 216, Fig. 4. The examiners asserted that the protein would be both an antigen and a hydrophobizing agent. Applicants representative discussed that this interpretation was not appropriate, and that arguments and possible clarifying amendments may be submitted in Applicants' response.

The subject matter of new claims 21-26 was discussed with the examiners, and the examiners appeared to agree that these changes would more particularly define the invention. For example, it was noted that a number of claims directed to features of the hydrophobized polysaccharide are not rejected over Kohno. However, the examiners indicated that the term alkyl may be broadly interpreted to include a protein attached to a polysaccharide. Again Applicants' representative indicated that arguments and possibly clarifying amendments would be submitted in the response.

The supervisor expressed her concern that the claims are directed to a cell, but she could not ascertain the structure of the cell in the claim. The supervisor appeared to be reading that the cell was separated from the hydrophobized polysaccharide and the antigen despite the fact that the claims do not recite such separation.

Regarding the obviousness rejections, Applicants representative repeated and emphasized arguments as previously submitted.

Arguments as presented during the interview are included in the remarks herein.

Withdrawal Of Finality Of Previous Office Action And Action On Each Of The Pending Claims

Applicants express appreciation for the withdrawal of finality of the previous Office Action and an action on the merits of each of the pending claims.

Information Disclosure Statement

Applicants express appreciation for the inclusion with the Office Action of an initialed copy of the Form PTO-1449 submitted with the Second Supplemental Information Disclosure Statement, filed July 2, 2004, whereby the Examiner's consideration of the disclosure statement is of record.

Rejections

The following rejections are set forth in the Office Action:

(a) Claims 13-14 are rejected under 35 U.S.C. 103(a) as obvious over Nestle et al. (hereinafter "Nestle"), Nature Medicine, Vol. 4, No. 3, pp. 328-332 (1998), in view of Jiang et al. (hereinafter "Jiang"), Nature, Vol. 375, 11 May 1995, pp. 151-155.

(2) Claims 1-3, 6, 11, 12, 15, 18 and 20 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kohno et al. (hereinafter "Kohno"), Cellular Immunology, 168, 211-219 (1996).

(3) Claims 1-20 are rejected under 35 U.S.C. 103(a) as obvious over Nestle et al. in view of Gu et al. (hereinafter "Gu"), Cancer Research 58, 3385-3390 (1998).

Prior to responding to the merits of each of the separate rejections, Applicants initially note that it appears that the Examiner is interpreting the language "hydrophobized

polysaccharide" in a broader manner then defined in Applicants' specification and disclosed in the prior art. For example, the rejection contends that pullulan or mannan are hydrophobized polysaccharides. However, a review of Applicants' specification, such as beginning at the bottom of page 6, indicates that polysaccharides such as pullulan and mannan are starting materials which are hydrophobized. Therefore, in contrast to the assertion in the rejection, it does not appear that any of Kohno, Nestle or Jiang discloses a hydrophobized polysaccharide, and would not teach or suggest the currently claimed cell formed by, for example, as recited in claim 11, reacting *in vitro* a complex with an antigen-presenting cell, said complex formed from interaction of a hydrophobized polysaccharide and an antigen.

During the above-noted interview, the examiners appeared to agree that Applicants' specification as well as the prior art of record supported Applicants' position that one having ordinary skill in the art would understand the meaning of the terminology "hydrophobized polysaccharide". However, as noted above, the examiners asserted that the protein of Kohno could be both an antigen and a hydrophobizing agent. Whether or not this is an accurate statement, the claims do not include such an interpretation. In this regard, for example, claim 1 recites a cell capable of inducing cellular immunity, the cell comprising an *in vitro* reaction product of a complex with an antigen-presenting cell, the complex formed from interaction of a hydrophobized polysaccharide and an antigen. Thus, according to Applicants' claims, the term "complex" is directed to a conjugate, e.g., an aggregate, formed from interaction of a hydrophobized polysaccharide and an antigen. The whole cell system is obtained by reaction of a complex, i.e., a result of formation of a particle using a hydrophobized polysaccharide and an antigen, with an

antigen-presenting cell. Certainly, Kohno does not disclose a complex formed from interaction of a hydrophobic polysaccharide and an antigen.

Response To Rejection Of Claims 13-14 Under 35 U.S.C. 103(a) As Obvious Over Nestle In View Of Jiang.

The rejection asserts that Nestle teaches a method of inducing cellular immunity comprising isolating a dentritic cell (DC) antigen presenting cell (APC), reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration.

The rejection contends that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to perform a method for inducing cellular immunity comprising isolating an APC, reacting the APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle, including a hydrophobized polysaccharide complex (such as mannan) in the reacting of the antigen with APC. The rejection attempts to support the addition of mannan complex to the reaction by asserting that the addition would have been expected to increase the uptake and presentation by the DC, given the teachings of Jiang that activation of the DC homolog of the macrophage mannose receptor (DEC-205) can facilitate a 100-foled increase in the uptake and presentation of the antigen by DC.

In response and as previously noted by Applicants, Applicants' rejected claims 13 and 14 include, amongst other features recited therein, a method for inducing cellular immunity *in vivo* comprising isolating an antigen-presenting cell from a living body and reacting a complex comprising a hydrophobized polysaccharide and an antigen with the

antigen-presenting cell. Applicants again respectfully submit that one having ordinary skill in the art would not have been motivated to combine the disclosures of Nestle and Jiang as asserted in the Office Action. However, even if for the sake of argument, the disclosures were combined, Applicants again respectfully submit that neither of Nestle nor Jiang discloses reacting a complex comprising a hydrophobized polysaccharide and an antigen with the antigen-presenting cell. Therefore, no combination of Nestle and Jiang would include a hydrophobized polysaccharide-antigen complex or reaction of a hydrophobized polysaccharide-antigen complex with an antigen-presenting cell.

For the sake of brevity, Applicants are not repeating the arguments already of record with respect to this ground of rejection, but incorporate such arguments by reference herein. In this regard, at least for the reason that neither Nestle nor Jiang discloses a hydrophobized polysaccharide, the rejection of record is without appropriate basis and should be withdrawn. Therefore, withdrawal of this ground of rejection is respectfully requested.

Response To Rejection Of Claims 1-3, 6, 11, 12, 15, 18 And 20 Under 35 U.S.C. 102(b) As Being Clearly Anticipated By Kohno.

For at least the reasons set forth above, Kohno does not teach or suggest each and every feature recited in Applicants' claims whereby this ground of rejection is without appropriate basis, and should be withdrawn.

Thus, Kohno does not teach, as recited in independent claim 1, a cell capable of inducing cellular immunity, said cell comprising an *in vitro* reaction product of a complex with an antigen-presenting cell, said complex formed from interaction of a hydrophobized

polysaccharide and an antigen; or as recited in claim11 a method for preparing a cell capable of inducing cellular immunity comprising reacting *in vitro* a complex with an antigen-presenting cell, said complex formed form interaction of a hydrophobized polysaccharide and an antigen; or as recited in claim 20, an *in vitro* cell capable of inducing cellular immunity, said *in vitro* cell comprising a complex comprising a combination of a hydrophobized polysaccharide, an antigen and an antigen-presenting cell.

Therefore, this ground of rejection should be withdrawn.

Response To Rejection Of Claims 1-20 Under 35 U.S.C. 103(a) As Obvious Over Nestle In View Of Gu.

In this ground of rejection, the rejection contends that it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to produce a product for, and perform a method for, inducing cellular immunity comprising isolating a DC APC, reacting said APC with a tumor antigen, and returning the resulting cell to the living body by parenteral administration, as taught by Nestle. The rejection further concludes that one of ordinary skill in the art at the time of the invention would have been motivated to employ the cholesterol bearing mannan polysaccharide complexed to an ErbB-2 antigen of Gu given the teaching of the reference that the ErbB-2– antigen is overexpressed in a wide range of human adenocarcnomas (and would thus provide an obvious target for immunotherapy) and that the use of the cholesterol bearing mannan polysaccharide facilitates the entry of the antigen into the MHC Class I pathway for presentation by APCs.

In response, the Examiner is reminded that Gu was utilized in the first Office Action in an anticipation rejection of claims 1-10, and Applicants provided remarks thereto in their response filed January 13, 2004. In particular, Applicants noted therein, and once again point out that Gu discloses a hydrophobized polysaccharide-antigen complex which is injected into an animal. Gu teaches the extraction of CTL's from the marrow of the inoculated animal. Thus, Gu relates to a hydrophobized polysaccharide-antigen complex which is injected into an animal, but does not teach or suggest (whether taken alone or combination with Nestle) Applicants products or methods.

To further denote the advantages of Applicants' claimed products and methods over a combination of Nestle and Gu, Applicants once again point to further information regarding the subject matter as disclosed in Gu. In particular, Applicants refer to the previously submitted Wang et al., International Journal of Oncology 14, 695-701, 1999 and Ikuta et al., Blood, 15 May 2002, Volume 99, No. 10. These documents were submitted with the January 13, 2004 Amendment, and resubmitted herewith for the convenience of the Examiner. Moreover, the documents are listed on the attached Form PTO-1449. The Examiner is respectfully requested to initial the form and forward the initialed form to Applicants.

In particular, Applicants' invention comprises the inclusion of an antigen-presenting cell with a complex comprising a hydrophobized polysaccharide and an antigen. As can be seen in Fig. 1 of Wang et al. (which is similar to Fig. 5 of Gu for CHM-HER2 instead of CHP-HER2 in Wang et al.) as compared to Fig. 5 of Wang et al., dentritic cell pretreated CHP-CAB complexes provide tumor suppression even after 10 days whereas unpretreated CHP-CAB complexes show tumor suppression through 3

days. This is further evidence of the structural and advantageous differences between Applicants' invention and that disclosed by Gu.

Accordingly, Applicants respectfully submit that the record is clear that Nestle does not teach or suggest any use of a hydrophobized polysaccharide; does not teach or suggest any use of a complex of a hydrophobized polysaccharide and an antigen; and does not teach or suggest any use of any type of combination of an antigen-presenting cell, a hydrophobic polysaccharide and an antigen. The record is also clear that Gu discloses hydrophobized polysaccharide-antigen complex which is injected into an animal, but does not teach or suggest an *in vitro* reaction product of a complex with an antigen-presenting cell, said complex formed from interaction a hydrophobized polysaccharide and an antigen such as recited in Applicants' claim 1.

Applicants respectfully submit that one having ordinary skill in the art would not combine the disclosures of Nestle and Gu as asserted in the rejection. In this regard, there is no motivation to incorporate hydrophobized polysaccharide-antigen complex which is disclosed in Gu in the process of Nestle. Moreover, there is no motivation to combine the disclosures to arrive at Applicants' claims. In any event, whether the disclosures are properly combinable or not, the advantageous results associated with Applicants' product and methods are not taught or suggested in the prior art of record.

With regard to the above, it appeared at the interview, that these arguments may be persuasive to the examiners of patentability of Applicants' invention. However, the examiners deemed that there may be a possible rejection based upon loading of APC *in vitro* versus injecting vaccine *in vivo*. Applicants note that such a rejection is not presently

of record, and it is not clear as to whether such a rejection will be presented. Therefore, Applicants reserve the right to address such a rejection if and when made.

Applicants once again also bring to the Examiner's attention that the hydrophobized polysaccharide according to the present invention can form a complex with a tumor antigen, whereas a polysaccharide in the prior art cannot form a complex with a tumor antigen. Thus, for this additional reason, the presently claimed invention would not have been obvious to one skilled in the art.

Therefore, Applicants respectfully submit that this rejection is without appropriate basis, and should be withdrawn.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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